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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,794	04/08/2005	Francis Thomas Boyle	100864-1P US	4278

44992 7590 09/12/2007
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EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1609	

MAIL DATE	DELIVERY MODE
09/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,794	BOYLE ET AL.	
	Examiner	Art Unit	
	Marcos L. Sznaidman	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,10 and 12-24* is/are pending in the application.

4a) Of the above claim(s) *12 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,10,13-19 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10 pages*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the following species: ZD4054 as the endothelin receptor antagonist, ZD1839 as the EGFR TKI, and lung cancer as the type of cancer in the reply filed on August 24, 2007 is acknowledged.

Status of claims

Claims 1-4, 6-7, 10 and 12-24 are currently pending and are the subject of this office action. Claims 5, 8-9 and 11 are cancelled. Claims 12 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 24, 2007. Claims 1-4, 6-7, 10, 13-19 and 21-24 are presently under examination.

Priority

The present application claims priority to foreign application: United Kingdom 0223854.1 filed on: 10/12/2002. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daub et. al. (Nature, 379 (1996) 557-560) in view of Bradbury et. al.

(US patent 6,258,817) and Tortora et. al. (Clinical Cancer Research 7, (2001) 4156-4163).

Claims 1-4, 6 and 17-18 are drawn to a composition comprising ZD4054 (an endothelin receptor antagonist) and ZD1839 (an EGFR TKI).

Daub et. al. teach that: mitogens such as ET-1 (an endothelin agonist), LPA and thrombin mediate cell proliferation through ligand-independent induction of tyrosine phosphorylation of the RTKs EGFR and p185 in Rat-1 fibroblasts (see page 560, first three lines of the next to last paragraph). They also say: more details of this RTK transactivation mechanism are needed to clarify its role in the regulation of biological processes and the pathophysiology of diseases such as cancer. These statements clearly suggest the use of a combination of an endothelin antagonist and an EGFR TK inhibitor for the treatment of cancer. Daub et. al. do not teach the use of the particular combination: ZD4054 (an endothelin receptor antagonist) and ZD1839 (an EGFR TKI). However, Bradbury et. al. teach the use of endothelin receptor antagonists in general (see abstract), and ZD4054 in particular (see claim3, lines 34 and 35) for medical treatments, and Tortora et. al. teach the use of ZD1839 for the treatment of cancer (see abstract).

Since Daub et. al clearly show that the mechanism of action of endothelin receptors and EGFR receptors are closely interrelated, suggesting that inhibition of both receptors might have a benefit in the treatment of cancer, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine two inhibitors of the above-mentioned receptors like ZD4054 (an endothelin receptor antagonist) and

ZD1839 (an EGFR TKI) for the treatment of cancer; thus resulting in the practice of instant claims 1-4, 6 and 17-18 with a reasonable expectation of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 10, 13-16, 19, and 21-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 7, 10, 13-16, 19, and 21-24 recite a method for treating lung cancer in a warm-blooded animal, such as man, in need of such treatment, which comprises administering to said animal an effective amount of the combination described above (ZD4054 and ZD1839). However the specification fails to disclose any data to support the fact that using this particular combination (or any combination) will result in an effective treatment of lung cancer (or any cancer). There is only experimental data that demonstrates the involvement of MAPK in both ET-1 and EGF osteoblastic signaling pathways, but no data in vivo or in vitro to support the claim that this particular combination could result in an effective treatment of lung cancer. There is also no

evidence in the prior art that a combination of any endothelin antagonist in combination with an EGFR TK inhibitor will result in the effective treatment of any type of cancer. For this reason, one skilled in the art could not use the invention of claims 7, 10, 13-16, 19, and 21-24, without undue experimentation.

Conclusion

No claims are allowed. Claims 1-4, 6 and 17-18 are rejected under 35 U.S.C. 103(a), and Claims 7, 10, 13-16, 19, and 21-24 are rejected under 35 U.S.C. 112, first paragraph.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcos L. Sznaidman whose telephone number is 571 270-3498. The examiner can normally be reached on Monday through Friday 9 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MLS
September 6, 2007

Cecilia J. Tsang
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